Knowledge update nuchal translucency as an antenatal screening test for cardiac defects

Paula Coles, Information Scientist
September 2012

SOURCES SEARCHED: Medline (OvidSP), Embase, and the Cochrane Library.

DATES OF SEARCH: January 2003 – September 2012

SEARCH STRATEGY:

1. exp Heart Defects, Congenital/ (112002)
2. ((heart or cardiac) adj (defect$ or anomal$ or malformation$ or abnormalit$)).tw. (17649)
3. coarct$tw. (7433)
4. (double outlet right ventricle or DORV).tw. (1244)
5. (double outlet adj2 ventricle).tw. (1290)
6. endocardial cushion defect.tw. (295)
7. ((left ventr$ outflow adj2 obstruct$) or LVOT$).tw. (2001)
8. ((interrupt$ adj3 aort$ heart) or IAA).tw. (3596)
9. (hypoplastic left heart or HLHS).tw. (3722)
10. ((mitral or aorti$) adj (atresia or stenosis)).tw. (16644)
11. PVOD.tw. (114)
12. Eisenmenger$ syndrome.tw. (658)
13. ((transposition adj3 great arter$) or TGA).tw. (7561)
14. (univentric$ heart or UVH).tw. (487)
15. single ventric$.tw. (2182)
16. (anomalous pulmonary adj2 drainage).tw. (639)
17. (anomalous pulmonary venous adj (return or connection)).tw. (1441)
18. (TAPVD or TAPVR or TAPVC or PAPVD or PAPVR).tw. (362)
19. (ventricular septal defect or VSD).tw. (9037)
20. (((atrioventricular or ventricular) adj septal defect) or VSD or AVSD).tw. (9683)
21. (pulmonary adj2 (atresia or stenosis)).tw. (6682)
22. (tricuspid adj2 stenosis).tw. (573)
23. tetralogy of fallot.tw. (5823)
24. patent ductus arteriosus.tw. (5625)
25. atrial septal defect.tw. (5933)
26. patent foramen ovale.tw. (2989)
27. ventricular septal defect.tw. (7873)
28. branch pulmonary artery.tw. (192)
29. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 (155329)
30. exp Prenatal Diagnosis/ (56233)
31. 29 and 30 (3608)
32. (screen$3 or detect$3 or test or tests or testing).tw. (2735789)
33. Mass Screening/ (75474)
34. 32 or 33 (2752939)
35. (pregnan$ or antenatal$ or prenatal$).tw. (386332)
36. exp Pregnancy/ (672396)
37. 35 or 36 (760234)
38. 31 or 38 (4457)
39. Nuchal Translucency Measurement/ (752)
40. nuchal translucency.tw. (1553)
41. 40 or 41 (1706)
42. 39 and 42 (263)
43. limit 42 to yr="2003 -Current" (194)

Similar searches were also carried out in Embase, and the Cochrane Library.
All searches carried out on 17 August 2012

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Inclusions and exclusions

The above search strategies retrieved 410 references in total. After duplicate references were removed a total of 293 potentially relevant references were left. The title and abstracts of the remaining citations were scanned for relevance to nuchal translucency as an antenatal screening test for cardiac defects.

63 references were deemed to be relevant and are classified in to the categories below. These references will be passed to the expert reviewer and assessed further for possible inclusion in the UK NSC review.

There will inevitably be some overlap between categories.

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These references are listed below. Abstracts have been provided where possible.

**Systematic reviews (5)**


Cardiac defects, the most common form of congenital anomaly, are found in 2-8 of every 1000 pregnancies. Increased nuchal translucency (NT) on ultrasound is an established marker for first-trimester detection of congenital heart defects (CHDs), with or without structural anomalies, in chromosomally normal and abnormal fetuses. However, due to modest sensitivity and specificity, many fetuses with increased NT who do not have CHD may undergo detailed cardiac scans. Moreover, NT screening may miss some fetuses with CHD and normal
karyotype. Ductus venosus (DV) Doppler waveform has been investigated to improve the diagnostic discrimination of ultrasound among cardiac anomalies in chromosomally abnormal and normal fetuses. DV has shown variable results in several studies in fetuses with normal karyotype; its value for identifying fetuses with CHD in the setting of a normal versus an increased NT is unclear. The aim of this meta-analysis was to evaluate the diagnostic performance of first-trimester DV for detection of CHD in chromosomally normal fetuses. A search of MEDLINE, ISI, SCOPUS, and EMBASE was performed for studies published between 1999 and 2011. Key words included "ductus venosus," "DV," "chromosomal abnormalities," "congenital heart disease," and "nuchal translucency." The diagnostic accuracy of DV was examined in 7 studies involving 50,354 fetuses with normal karyotype regardless of NT status, 9 studies including 2908 fetuses with increased NT, and 7 studies involving 47,610 fetuses with normal NT. Hierarchical summary receiver operating characteristic curves were drawn based on parameters of the fitted models. Analysis of the hierarchical summary receiver operating characteristic curves showed that the sensitivity and specificity of DV to detect CHD in the normal karyotype population regardless of the NT status were 0.50 and 0.93, respectively. Summary sensitivity and specificity were 83% and 80% among participants with increased NT, and 19% and 96% among those with normal NT, respectively. The findings of this meta-analysis showing the estimated performance of DV for detecting CHD in chromosomally normal fetuses should be considered in evaluating the potential use of this screening test and its limitations. 2012 Lippincott Williams & Wilkins, Inc.


OBJECTIVE: To review literature about the efficacy of early ultrasound (EU) at 11-14 weeks to identify fetal malformations. STUDY DESIGN: A search in PubMed, Medline, Embase, Cochrane was performed (1999-2009). Key words: fetal anatomy, fetal echocardiography, nuchal translucency, fetal malformations, prenatal diagnosis, prenatal screening, first trimester ultrasound. Inclusion criteria were fetal anatomy examination at EU early diagnosis of fetal malformations confirmed by 18-22 weeks ultrasound, postnatal, or postmortem examination. Data were abstracted following PRISMA guidelines. Pooled sensitivity (Sv-95%CI) and specificity (Sp-95%CI) were calculated by DerSimonian-Laird method, RESULTS: Twelve articles pooled 324/20,962 (15:1.000) malformed fetuses. Sv and Sp were 48%-43-54 and 100%-100-100 respectively. The highest Sv was observed for neck anomalies (100%-69-100), followed by anomalies of the brain and spine (68%-51-82), abdomen (64%-31-89), heart (56%-47-65), limbs (50%-25-75), and genitourinary tract (24%-7-50). Sp was 100% (100-100) in all types of structural anomalies. Genitourinary system presented the highest inter-studies variability, ranging Sv from 0 to 100%. Sv was 49%-41-58 for isolated and 56%-42-68 for associated anomalies. Sp was 100%-98-100 for both isolated and associated anomalies. 2,121 high-risk and 18,508 low-risk women were identified. In the former, Sv and Sp were 66%-55-75 and 100%-99-100. In the latter, Sv and Sp were 40%-34-47 and 100%-100-100 respectively. Echocardiography was more sensitive (58%-47-69) than complete ultrasound (52%-44-59) in identifying congenital heart defects. Sv for identification of cardiac defects mildly increased when echocardiography was supplemented by Doppler examination (56%-44-67) as compared with examination of fetal heart without Doppler interrogation (52%-45-60). CONCLUSIONS: Doppler examinations, the presence of risk factors and associated anomalies improved the accuracy of EU. Because of the natural history of fetal defects and the late development of some organ systems, a number of fetal anomalies remains undetected by EU.

3. Papatheodorou SI, Evangelou E, Makrydimas G, et al. First-trimester ductus venosus screening for cardiac defects: A meta-analysis. BJOG: An International Journal of Obstetrics and Gynaecology 2011;118 (12):1438-45. Background Heart defects are the most common congenital abnormalities. Objective We aimed to evaluate in a meta-analysis the screening performance of abnormal ductus venosus (DV) Doppler waveform for detection of congenital heart disease (CHD) in chromosomally normal fetuses. Search strategy Studies were retrieved from a search of MEDLINE, ISI, SCOPUS and EMBASE (from 1999 to March 2011) using the keywords 'ductus venosus', 'DV', 'chromosomal abnormalities', 'congenital heart disease' and 'nuchal translucency'. Selection criteria We considered all studies that examined the diagnostic performance of DV in the first trimester for CHD in chromosomally normal fetuses. We included studies that were limited to fetuses with increased nuchal translucency (NT), normal NT, and studies that examined fetuses regardless of NT status. Data collection and analysis Seven studies (n = 50 354) regardless of the NT status, nine studies (n = 2908) with increased NT and seven studies (n = 47 610) with normal NT were included in the meta-analysis. We drew hierarchical summary
receiver operating characteristic (HSROC) curves using the parameters of the fitted models. Main results In populations including participants regardless of NT status, the summary sensitivity and specificity of DV for detecting CHD were 50 and 93%, respectively. In participants with increased NT, the summary sensitivity and specificity were 83 and 80%, and in those with normal NT, they were 19 and 96%, respectively. Authors’ conclusions The estimated performance of DV assessment for detection of CHD in chromosomally normal fetuses can be considered in evaluating the potential use and limitations of this screening test. 2011 The Authors BJOG An International Journal of Obstetrics and Gynaecology 2011 RCOG.


Objectives: To assess the performance of nuchal translucency (NT) measurements in screening for congenital heart defects (CHD) which would benefit from prenatal detection. Methods: A literature search was conducted of studies published prior to August 2007 of CHD and NT measurements in fetuses without chromosome defects. From this, data on 159 pregnancies were obtained. Fetuses with CHD that would benefit from prenatal detection were identified and their NT measurements were compared with NT measurements in 29 776 unaffected fetuses without Down syndrome from the Serum Urine and Ultrasound Screening Study (SURUSS) trial to determine the screening performance of NT measurements. Results: In all 67 fetuses with CHD were identified as potentially likely to benefit from prenatal detection. Using NT measurements, the estimated detection rate (DR) for a 5% false-positive rate (FPR) was 52% (95% CI: 42-71). Conclusion: Prenatal screening for CHD using NT measurements is likely to be effective, and given that NT measurement is already in place as part of prenatal screening for Down syndrome; this is an ideal time to set up demonstration projects to validate these results. Copyright 2008 John Wiley & Sons, Ltd.


OBJECTIVE: The purpose of this study was to evaluate the screening performance of increased first-trimester nuchal translucency for the detection of major congenital heart defects. STUDY DESIGN: A meta-analysis based on MEDLINE and EMBASE searches (up to June 2002) that assessed the diagnostic performance of increased nuchal translucency for congenital heart defect detection. Weighted sensitivity and specificity estimates (random effects) and summary receiver-operating characteristic curves were obtained. RESULTS: Eight independent studies with 58,492 pregnant women were analyzed. There was significant heterogeneity among the studies. Nuchal translucency above the 99th percentile had a sensitivity of 31% and specificity of 98.7% (random effects calculations), with a positive likelihood ratio of 24. Summary receiver-operating characteristic estimates were consistent with these values. The ability of nuchal translucency measurements above this threshold to detect cardiac malformations varied nonsignificantly (P = .64) for different congenital heart defects types (sensitivity range, 25%-55%). CONCLUSION: Nuchal translucency screening is a modestly efficient strategy for congenital heart defect detection; the use of the 99th percentile threshold may capture approximately 30% of congenital heart defects.

Non-systematic reviews (6)


Sonographic assessment of fetal nuchal translucency (NT) thickness is the cornerstone of screening for chromosomal abnormality at 11-13<sup>+</sup>6<sup>-</sup> weeks gestation. This marker was first recognized in pregnancies being karyotyped for advanced maternal age, but its underlying pathophysiology remains to be fully determined. Although increased NT is clearly associated with changes in both lymphatic and cardiac development, neither is an obvious causative agent. The association with cardiac defects has now being subjected to a significant amount of research, with a large body of evidence showing that this marker is also a screening tool for major cardiac defects - although it performs more modestly than for chromosomal abnormality. The field continues to change rapidly. Recent evidence that uses a combination of increased NT, tricuspid regurgitation and abnormal flow in the ‘a’ wave of the ductus venosus can provide an effective screening strategy to predict many major cardiac defects at this early stage of pregnancy. 2012.

A new approach of prenatal care would calculate patientspecific risk for different pregnancy complications, such as fetal abnormalities, miscarriage, fetal death, preeclampsia or fetal growth restriction. The visits for each patient would be scheduled according to the patient-specific and disease-specific risks. Doppler ultrasound of different maternal and fetal vessels, together with maternal history, serum biochemical and biophysical markers contribute in the prediction of different adverse pregnancy outcomes. Prediction of chromosomal abnormalities: Effective screening for chromosomal abnormalities is provided by a combination of maternal age, fetal nuchal translucency (NT) thickness and maternal serum PAPP-A and free beta-hCG, with a detection rate of 90% for a false positive rate of 5%. The addition of other Doppler ultrasound markers such as ductus venosus flow, tricuspid regurgitation or hepatic artery flow can improve the detection rate up to 95% reducing the false positive rate (FPR) up to 2.5%. Prediction of structural abnormalities: cardiac defects: The risk of congenital heart defects increases with NT measurement at 11-13 weeks and is higher in the presence of abnormal ductus venosus flow or tricuspid regurgitation. The combination of NT, ductus venosus and tricuspid flow could identify 50% of defects increases with NT measurement at 11-13 weeks and is higher in the presence of abnormal ductus venosus flow associated with a higher incidence of placental impairment, fetal growth restriction (FGR), and maternal and fetal factors. After adjusting for these factors, uterine artery pulsatility index (PI) is converted into multiple of the median (MoM) of the normal pregnancies. Algorithms that combine maternal characteristics, biophysical (including uterine artery PI) and biochemical factors could potentially identify about 90, 80 and 60% of pregnancies that subsequently develop early, intermediate and late PE, with a FPR of 5%. Fetuses with a birth-weight below the 5th centile are at increased risk of fetal death and handicap. Prenatal identification of these pregnancies reduces significantly these risks. Screening for FGR in the absence of preeclampsia by a combination of maternal factors, and biochemical and biophysical markers, including uterine artery PI, could potentially identify 75% of pregnancies delivering FGR fetuses before 37 weeks and 45% of those delivering at term.


Purpose of review: First trimester screening is presently offered to all pregnant women as a means of prenatal screening for Down syndrome, trisomy 18, and trisomy 13. Nuchal translucency measurement is a fundamental component of the screening protocol. A woman whose fetus' nuchal translucency is greater than the 95th percentile is also at increased risk for a multiplicity of other adverse pregnancy and pediatric outcomes, and as a consequence, counseling of patients about their testing options and range of pregnancy outcomes has become complex and difficult. Recent findings: The increased risk for chromosome abnormalities, congenital heart malformations, and pregnancy loss in the presence of an increased nuchal translucency is well documented. What has not been clearly defined is the incidence of other genetic syndromes, congenital defects, and adverse pregnancy and pediatric outcomes in the presence of increased nuchal translucency. Currently, Noonan syndrome is the only molecular genetic condition that has been shown to have a clear association with the finding of increased nuchal translucency in the first trimester. Summary: This article reviews the current literature on outcomes in pregnancies with an increased nuchal translucency and a normal karyotype. We summarize the range of outcomes detected in the first trimester with recommendations for further prenatal testing and counseling of patients. 2012 Wolters Kluwer Health | Lippincott Williams & Wilkins.


Nuchal translucency (NT) measurement between 11 and 14 weeks' gestation is an undisputed marker for aneuploidies. When conventional karyotyping is normal, enlarged NT is a strong marker for adverse pregnancy outcome, associated with miscarriage, intrauterine death, congenital heart defects, and numerous other structural defects and genetic syndromes. The risk of adverse outcome is proportional to the degree of NT enlargement. Although the majority of structural anomalies are amenable to ultrasound detection, unspecified genetic syndromes involving developmental delay may only emerge after birth. Concern over these prenatally
undetectable conditions is a heavy burden for parents. However, following detection of enlarged NT the majority of babies with normal detailed ultrasound examination and echocardiography will have an uneventful outcome with no increased risk for developmental delay when compared to the general population. Counseling should emphasize this to help parents restore hope in normal pregnancy outcome and infant development. (c) 2010 John Wiley & Sons, Ltd. [References: 58]


In this overview the current knowledge of the relationship between an increased nuchal translucency (NT) measurement and fetal heart structure and function in chromosomally normal fetuses is reviewed. Relevant pathophysiological theories behind the increased NT are discussed. Fetuses with an increased NT have an increased risk for congenital heart disease (CHD) with no particular bias for one form of CHD over another. This risk increases with increasing NT measurement. Although the NT measurement is only a modestly effective screening tool for all CHD when used alone, it may indeed be effective in identifying specific CHD “likely to benefit” from prenatal diagnosis. The combination of an increased NT, tricuspid regurgitation and an abnormal ductus venosus (DV) Doppler flow profile, is a strong marker for CHD. A fetal echocardiogram should be performed at 20 weeks’ gestation in fetuses with an NT >=95th percentile but <99th percentile. When the NT measurement is >=99th percentile, or when tricuspid regurgitation and/or an abnormal DV flow pattern is found along with the increased NT, an earlier echocardiogram is indicated, followed by a repeat scan at around 20 weeks’ gestation. The resultant increased demand for early fetal echocardiography and sonographers with this special expertise needs to be planned and provided for. Copyright 2009 John Wiley & Sons, Ltd.


Most obstetrical practices in the United States offer pregnant women at least one ultrasound during pregnancy. This prenatal ultrasound is usually scheduled at around 18 to 20 weeks gestation. Both the American Institute of Ultrasound in Medicine and the American College of Obstetricians and Gynecologists recommend that the four-chamber view be included to screen for congenital heart disease. Recently, many investigators have attempted to screen for congenital heart disease earlier in pregnancy. Fetal nuchal translucency thickness traditionally used to screen for fetal aneuploidy by transvaginal and abdominal ultrasound has also been shown to identify a large proportion of fetuses with congenital heart disease. Recent studies have also reported congenital heart disease in chromosomally normal fetuses with increased nuchal translucency thickness in the first trimester. Advances in ultrasound technology and training over the last 10 years allow greater visualization rates of the four-chamber view and outflow tracks in the late first trimester (up to 90% visualization at 13 weeks). Fetal echocardiography in the first trimester may be indicated for fetuses at risk for congenital heart disease. In this article we present a review of the most recent and ongoing clinical and basic research to support an earlier first trimester approach to diagnosing congenital heart defects.

Detection of cardiac anomalies by nuchal translucency (19)


Basics: The association of an increased nuchal translucency (NT) in the first trimester with a higher prevalence of fetal complex structural cardiac defects, in the absence of chromosomal abnormalities, has long being reported. The purpose of this study was to test the hypothesis that there is association between a borderline or increased NT (2mm or more) in 11+0-13+6 weeks euploid fetuses and a later diagnosis of isolated VSD. Methods: A case-control study was designed. 5464 second or third-trimester consecutive fetuses without extracardiac abnormalities and no cardiac anomalies other than a VSD were assessed in a period of two years. NT had been obtained between 11+0 and 13+6 weeks of gestation. A fetal echocardiogram and a morphological scan were performed, searching for the diagnosis of VSD and to exclude associated cardiac and noncardiac malformations. Fetuses with an altered karyotype or a postnatal diagnosis of chromosome abnormalities were excluded. Statistical analysis used Fisher’s exact test and ROC curves. Results: Mean maternal age was 32+-/5 years (21-42 years) and gestational age at the time of the fetal echocardiogram was 25+/6 weeks (19-31 weeks). Mean NTwas 2.2 in fetuses with VSD and 1.4 without. Out of 319 fetuses with a NT of 2mm or more, 67 had a VSD (52
muscular and 15 perimembranous) (21%), while in only 115 out of 5180 fetuses with a NT<2.0mm a VSD was detected (86 muscular and 29 perimembranous) (2.2%) (p<0.0005), being the relative risk59.3 (99% CI: 6.5-13.5). A ROC curve determined the cut-off value of NT (2.0), with a sensitivity of 48.3% and a specificity of 91.4%, with an area under the curve50.695 (p<0.0001). Conclusions: Fetuses without chromosome abnormalities with a first trimester NT of 2mm or more have an 8.3-fold increase in the risk of presenting an isolated ventricular septal defect. We speculate that the defects could have been larger and functionally important in the first trimester, increasing the NT as a consequence of hemodynamic overload and gradually decreasing its diameter until the second and third trimesters. This knowledge may have implications in prenatal management and counseling.


OBJECTIVE: We sought to evaluate cutoff levels for first trimester nuchal translucency (NT) measurements and abnormal cardiac findings (ACF) detected on second trimester ultrasound in chromosomally normal fetuses.

STUDY DESIGN: We performed a retrospective analysis of singleton pregnancies seen in our ultrasound unit between 1/1/06-1/30/10 for an NT screen [11-1/7 weeks - 13-6/7 weeks] and follow-up second trimester scan [17-0/7 weeks - 22-6/7 weeks]. Cases with an abnormal karyotype by chorionic villus sampling or amniocentesis were excluded. The NT was measured according to published guidelines. We determined the 95 percentile (%ile) for our center using gestational age specific NT MoMs. Detection and false positive rates were based on ACF detected in the second trimester.

RESULTS: There were 3,950 chromosomally normal singleton pregnancies, of which 16 cases of ACF were identified in the second trimester ultrasound (4.1/1000). The 16 cardiac abnormalities included: 10 (62.4%) ventricular septal defects, 3 (18.8%) hypoplastic left ventricle and 3 (18.8%) other. The mean (+/-SD) NT for the normal and ACF cases in the second trimester were 1.8 (+/-0.5)mm and 2.3 (+/-0.9) mm, respectively (P<0.0001). With a NT measurement of 2.0 mm, the incidence of ACF was 8 of 2582 second trimester ultrasound (3.1/1000). The 95%ile MoM cutoff was 1.402. Of the cutoff points evaluated, the <95%ile was the most efficacious (Table 1). CONCLUSIONS: Increased first trimester NT measurement was associated with a higher risk of ACF in the second trimester scan in chromosomally normal fetuses. Using the 95%ile MoM was more efficacious than a cutoff based on mm. Patients with unexplained elevations of NT should be referred for a fetal echocardiogram. (Table presented).


OBJECTIVES: (1) Assess sensitivity of the measurement of nuchal translucency (NT), for the prenatal screening of congenital heart defect (CHD) on population-based data; (2) examine whether the sensitivity of NT varies for specific types of cardiac defects. METHODS: Using population-based data of the Paris Registry of Congenital Malformation for 935 fetuses with CHD and without chromosomal anomalies for the period 2001 to 2007, we calculated sensitivity of NT, its positive predictive value and likelihood ratio, for all CHD and for six types of CHD.

RESULTS: Sensitivity of NT was 7.1 and 4.2% for the 2.5 and 3.5 mm cut-off values, respectively; when isolated ventricular septal defects were excluded, sensitivity increased to 9.9 and 6.3%. Positive predictive values were 1.1 and 3.2% for 2.5 and 3.5 mm cut-offs, respectively. Of the six defects examined, sensitivity of NT was highest for heterotaxy followed by hypoplastic left heart syndrome and coarctation of aorta. CONCLUSION: Prevalence of CHD was about fourfold higher for fetuses with NT<3.5 mm (3.2%) than in the general population. This higher risk is comparable to that of other risk factors commonly used for early referral to specialized echocardiography. Nevertheless, our results, suggest that NT is not a very effective or efficient tool for the prenatal screening of CHD. Copyright Copyright 2011 John Wiley & Sons, Ltd.


Brief introduction: The ultrasound measurement of the nuchal translucency (NT) represents an important screening test to identify fetuses at higher risk for aneuploidies. Recently studies showed that an enlarged NT could be associated to Congenital Heart Diseases (CHD). The purpose of this study was to assess the accuracy of
NT values as a sonographic marker to screen CHD. Materials and Methods: In this retrospective study we report 75 pregnancies referred to prenatal diagnosis centre from 2007 to 2009 with fetuses with an increased NT (>95th percentile) not associated with other risk factors for heart anomalies. We define 2 study groups: group A includes 57 fetuses with a borderline increased NT from >95 to < 99 percentile; group B includes 18 cases with NT value > 99 percentile. Clinical cases or summary results: In the first group (A) we found 1 case (3.5%) of tetralogy of Fallot associated with aneuploidy. In the second group (B) we identified 4 cases (22.2%) of hypoplastic left heart syndrome and 1 case (5.5%) of ventricular septal defect. One case of hypoplastic left heart syndrome was associated with chromosomal aberration (5.5%), 2 cases presented others malformations (11.1%). Conclusions: Our findings suggests the importance of an echocardiographic study of the fetal heart morphology in all fetuses with an increased NT because of the high risk of fetal cardiac malformations in these pregnancies compared with general population.


Objectives: Our aims were to estimate the prevalence of increased nuchal translucency in fetuses with a normal karyotype that were subsequently diagnosed with congenital cardiac disease on fetal echocardiography, and to assess whether there is a link between increased nuchal translucency and specific congenital cardiac malformations. Methods: We reviewed all patients referred to Kings College Hospital and the Evelina Childrens Hospital in London for fetal echocardiography between January 1998 and December 2007. We investigated the proportion of chromosomally normal fetuses with congenitally malformed hearts in which nuchal thickness was increased, both overall and with specific defects. Results: We indentified 2133 fetuses with congenital cardiac disease by prenatal echocardiography. Of those, 707 were excluded due to abnormal karyotype, and 690 were excluded due to unknown karyotype. The remaining 736 were eligible for inclusion. Among 481 fetuses with documented congenital cardiac disease and normal chromosomes, making up 23% of the overall cohort, 224 had increased nuchal thickness defined as equal or greater than 2.5 millimetres, this being 0.47 of the inclusive cohort, with 95% confidence intervals from 0.42 to 0.51. These proportions were significantly higher than the expected proportion of the normal population, which was 0.05 (p < 0.001). The only diagnosis for which the proportion of fetuses with nuchal translucency measurement equal or greater than 2.5 millimetres was higher than the others was atrioventricular septal defect, with 0.62 of this cohort having abnormal values, with 95% confidence intervals from 0.47 to 0.77 (p = 0.038). Conclusion: We found that nearly half of prenatally diagnosed fetuses with congenitally malformed hearts, when examined ultrasonically in the first or early-second trimester, had increased nuchal thickness. We recommend, therefore, referral of all fetuses with increased nuchal translucency for fetal echocardiography. Copyright 2009 Cambridge University Press.


Objective: To determine fetal aneuploidy and to assess the value of increased nuchal translucency (NT) to detect congenital cardiac defects (CCD) at 11-14 weeks of gestation. Material and Methods: Nine hundred and fifty six women at 11-14 weeks of gestation were enrolled. Screening was performed by calculating the risk from maternal and gestational age, which was adjusted with the NT measurement and maternal serum biochemical markers. An adjusted risk of >1:270 was considered a positive screening test in which case fetal karyotyping was recommended. In cases where the NT was >=99<sup>th</sup> percentile for gestational age, echocardiography was performed. All infants underwent examinations for cardiac defects after birth. Results: Screening was positive in 21% (203/956) of fetuses. Fetal karyotyping was determined prenatally in 123 (12.9%) cases. Screening test displayed 60% sensitivity, 78.9% specificity, 1.48% positive predictive value (PPV) and 99.7% negative predictive value (NPV) for detecting fetal aneuploidies. For detection of cardiac anomalies, increased nuchal translucency had 28.6% sensitivity, 82.08% specificity, 1.16% PPV and 99.26% NPV. The overall diagnostic value of an increased NT for detection of CCD was 81.7%. Conclusion: Screening for fetal aneuploidy by maternal age, nuchal translucency and serum marker measurements can be effective for the detection of fetal abnormalities and during first trimester screening for aneuploidy, fetuses with increased transclucencies must be monitored closely with prenatal echocardiography. Copyright 2009 by Turkiye Klinikleri.


OBJECTIVE: To investigate the congenital heart disease (CHD) found in association with an increased nuchal
translucency (NT) at 11-14 weeks of gestation in chromosomally normal and abnormal fetuses. METHODS: Patients referred from January 1998 until May 2007 with an increased NT (> or = 95th percentile) where CHD was diagnosed were included. Chromosome analysis, fetal and postnatal echocardiography were performed. A postmortem examination followed pregnancy termination when possible. RESULTS: Major CHD was identified in 68 of 967 fetuses with an increased NT (median NT 4.8 mm, range 2.5-22 mm). Major CHD was found in 34 of 693 fetuses (4.9%) with a normal karyotype and increased NT (median 5.2 mm, range 2.5-9.6 mm). CHD frequency increased from 1.9%, with NT between 2.5 and 3.5 mm, to 27.7% when NT was > or = 6.5 mm. Septal defects predominated (20%) when NT was < or = 3.5 mm. With NT > 3.5 mm an equal distribution of CHD types was seen. Major CHD was identified in 34 of the 274 fetuses with an abnormal karyotype and increased NT (median 4.2 mm, range 2.5-22 mm). CONCLUSIONS: A variety of CHD is associated with an increased NT in the first trimester of pregnancy. Conotruncal defects, branchial arch derivative defects, left and right obstructive lesions (inflow and outflow) and shunts were seen. Copyright (c) 2008 John Wiley & Sons, Ltd.


OBJECTIVE: To estimate whether nuchal translucency assessment is a useful screening tool for major congenital heart disease (CHD) in the absence of aneuploidy. METHODS: Unselected patients with singleton pregnancies at 10 to 13 weeks of gestation were recruited at 15 U.S. centers to undergo nuchal translucency sonography. Screening characteristics of nuchal translucency in the detection of major CHD were determined using different cutoffs (2.0 or more multiples of the median [MoM], 2.5 or more MoM, 3.0 or more MoM). RESULTS: A total of 34,266 euploid fetuses with cardiac outcome data were available for analysis. There were 224 cases of CHD (incidence 6.5 per 1,000), of which 52 (23.2%) were major (incidence 1.5 per 1,000). The incidence of major CHD increased with increasing nuchal translucency: 14.1 per 1,000, 33.5 per 1,000, and 49.5 per 1,000 at 2.0 or more MoM, 2.5 or more MoM, and 3.0 or more MoM cutoffs, respectively. Sensitivity, specificity, and positive predictive values were 15.4%, 98.4%, and 1.4% at 2.0 or more MoM; 13.5%, 99.4%, and 3.3% at 2.5 or more MoM; and 9.6%, 99.7%, and 5.0% at 3.0 or more MoM. Nuchal translucency of 2.5 or more MoM (99th percentile) had a likelihood ratio (95% confidence interval) of 22.5 (11.4-45.5) for major CHD. Based on our data, for every 100 patients referred for fetal echocardiography with a nuchal translucency of 99th percentile or more, three will have a major cardiac anomaly. CONCLUSION: Nuchal translucency sonography in the first trimester lacks the characteristics of a good screening tool for major CHD in a large unselected population. However, nuchal translucency of 2.5 or more MoM (99th percentile or more) should be considered an indication for fetal echocardiography. 2007 The American College of Obstetricians and Gynecologists.


Objective: To assess the performance of nuchal translucency (NT) measurement in the first trimester of pregnancy as a marker for congenital heart defects (CHD) in the fetus in a low-risk obstetric population. Methods: Nuchal translucency screening was offered over a 3-year period to consecutive pregnant women without known a priori risk factors and attending midwife practices in three different areas in the Netherlands. In chromosomally normal fetuses and infants from the study population the NT measurements were matched with CHD detected either prenatally or postnataally. Results: NT screening was offered to 6132 women with an uptake of 83%. A total of 4876 NT measurements was performed. Pregnancy outcome data were available in 4181 cases (86%). Defects of the heart and great arteries (CHD) were diagnosed in 24 cases (prevalence 5.8/1000). Thirteen of these were classified as major (prevalence 3.1/1000). Two major CHD occurred in fetuses showing an increased NT at the first-trimester scan. The sensitivity of NT measurement >95th and >99th percentile for all CHD and for major CHD, was 8% and 15%, respectively. The positive likelihood ratios of NT > 95th <sup>th</sup> and >99th percentile for major CHD were 6, 5 and 33, respectively. Conclusion: In pregnancies without known risk factors also, an increased NT is associated with major cardiac defects in the fetus and therefore represents an indication for specialized fetal echocardiography. However, this association is too weak to envisage a role for NT measurement as single screening strategy for the prenatal detection of cardiac defects. Copyright 2007 John Wiley & Sons, Ltd.


Objective: To compare the rate of prenatal diagnosis of heart malformations between two policies of screening
for heart malformations. Design: Randomised controlled trial. Setting: Six university hospitals, two district general hospitals. Sample: A total of 39 572 unselected pregnancies randomised to either policy. Methods: The 12-week policy implied one routine scan at 12 weeks including measurement of nuchal translucency (NT), and the 18-week policy implied one routine scan at 18 weeks. Fetal anatomy was scrutinised using the same checklist in both groups, and in both groups, indications for fetal echocardiography were ultrasound findings of any fetal anomaly, including abnormal four-chamber view, or other risk factors for heart malformation. In the 12-week scan group, NT >=3.5 mm was also an indication for fetal echocardiography. Main outcome measure: Prenatal diagnosis of major congenital heart malformation. Results: In the 12-week scan group, 7 (11%) of 61 major heart malformations were prenatally diagnosed versus 9 (15%) of 60 in the 18-week scan group (P= 0.60). In four (6.6%) women in the 12-week scan group, the routine scan was the starting point for investigations resulting in a prenatal diagnosis versus in 9 (15%) women in the 18-week scan group (P= 0.15). The diagnosis was made <=22 weeks in 5% (3/61) of the cases in the 12-week scan group versus in 15% (9/60) in the 18-week scan group (P= 0.08). Conclusions: The prenatal detection rate of major heart malformations was low with both policies. The 18-week scan policy seemed to be superior to the 12-week scan policy, although the differences in prenatal detection rates were not statistically significant.


11. Westin M, Saltvedt S, Bergman G, et al. Is measurement of nuchal translucency thickness a useful screening tool for heart defects? A study of 16 383 fetuses. Ultrasound in Obstetrics and Gynecology 2006;27 (6):632-39. Objective: To determine the performance of nuchal translucency thickness (NT) measurement as a screening method for congenital heart defects (CHD) among fetuses with normal karyotype. Methods: An NT measurement was made in 16383 consecutive euploid fetuses derived from an unselected pregnant population. The cut-offs for increased risk of heart defects, chosen a priori and tested prospectively, were: NT > 95<sup>th</sup> centile for crown-rump length, NT >= 3 mm, and NT >= 3.5 mm. The sensitivity and false-positive rate (FPR; 1 minus specificity) of the risk cut-offs and their positive and negative likelihood ratios (+LR and -LR) with regard to CHD were calculated. Results: Among the 16383 fetuses with an NT measurement there were 127 cases with a diagnosis of heart defect confirmed by cardiac investigations after birth or at autopsy. Of these, 55 defects were defined as major, of which 52 were isolated (no other defects or chromosomal aberrations), corresponding to a prevalence of major heart defects in chromosomally normal fetuses/newborns of 3.3/1000. The sensitivity, FPR, +LR and -LR for NT >= 95<sup>th</sup> centile for crown-rump length, NT >= 3 mm, and NT >= 3.5 mm were: 13.5%, 2.6%, 5.2 and 0.9, respectively. For NT >= 3.0 mm these values were: 9.6%, 0.8%, 12.0 and 0.9, and for NT >= 3.5 mm they were: 5.8%, 0.3%, 19.3 and 0.9. Conclusions: NT measurement is a poor screening method for isolated major CHD. A method with a much higher detection rate and with a reasonably low FPR is needed. However, increased NT indicates increased risk of fetal heart defect, and women carrying fetuses with increased NT should be offered fetal echocardiography in the second trimester. Copyright 2006 ISUOG. Published by John Wiley & Sons, Ltd.

12. Bruns RF, Moron AF, Murta CGV, et al. The role of nuchal translucency in the screening of congenital heart defects. [Portuguese, English]. Arquivos brasileiros de cardiologia 2006;87 (3):272-79+307-14. OBJECTIVE: Assess the accuracy of the nuchal translucency (NT) measurement between 11 and 13 weeks and 6 days of gestation as a sonographic marker to screen for congenital heart defects (CHD). METHODS: This is a multi-center retrospective study in which singleton gestations of euploid fetuses were analyzed. NT measurement was performed in the first trimester examination when the fetal crown-rump length (CRL) was 45 to 84 mm, according to the criteria established by the Fetal Medicine Foundation. The cases were followed up to one month postpartum to assess the presence of CHD. RESULTS: Three thousand six hundred and sixty four gestations were analyzed, of which twenty newborn infants had some congenital heart defect up to the first month of life (prevalence of 0.55%). The median NT in fetuses with CHD was 1.70 mm, and 1.60 mm in fetuses without CHD. However no statistically significant difference was observed between the two medians (Mann-Whitney test, p > 0.05). The NT sensitivity to detect CHD ranged from 15% to 20%, with a probability of false positive cases of 86.4% to 97.9%, depending on the cut-off point used. Odds ratio for CHD was high when compared to the classical indications for fetal echocardiography, ranging from 4.7 to 33.7, according to the cut-off point used. CONCLUSION: Despite the low sensitivity of the test, increased NT is an important risk factor for CHD, and should be included in the strategy of prenatal screening for these diseases.

**OBJECTIVE:** Increased fetal nuchal translucency is associated with increased risk for congenital heart defects. In the present study, we aimed to investigate whether fetal nuchal translucency distribution differs among different types of congenital heart defects and whether it can lead to an earlier diagnosis. **STUDY DESIGN:** Four fetal echocardiography units provided data on fetuses with a congenital heart defect diagnosis in whom nuchal translucency thickness had been measured in the first trimester. Nuchal translucency data were compared per chromosomal status and type of congenital heart defect. Data on gestational age at diagnosis were also analyzed. **RESULTS:** Six hundred thirty-seven cases of congenital heart defect with known karyotype and exact nuchal translucency measurements were analyzed. Nuchal translucency was > or =3.5 mm in 22.9% of chromosomally normal fetuses (n = 397) and 58.8% of chromosomally abnormal cases (n = 240). Among fetuses with normal karyotype, the proportion of cases of congenital heart defect with increased nuchal translucency was similar in each of the subtypes of congenital heart defect (P = .96). Mean gestational age at diagnosis of congenital heart defect in fetuses with normal karyotype was 22.1 weeks with nuchal translucency of <3.5 mm and 16.1 weeks with nuchal translucency of > or =3.5 mm. **CONCLUSION:** Finding nuchal translucency of > or =3.5 mm may lead to an earlier diagnosis of all major types of congenital heart defects.


**OBJECTIVE:** We sought to evaluate the association between first trimester nuchal translucency measurement and the risk for major congenital heart defect in chromosomally normal fetuses. **STUDY DESIGN:** First trimester (10 weeks 4 days of gestation to 13 weeks 6 days of gestation) nuchal translucency was obtained in a large prospective multicenter National Institute of Child Health and Human Development study for Down syndrome prediction. The study, which was conducted between May 1998 and December 2000, was restricted to singleton pregnancies. Gestational age was determined by crown rump length measurements. Perinatal outcomes were determined and included the frequency of major congenital heart defect, which was defined as those cases that potentially could require surgery, intensive medical therapy, or prolonged follow-up time. Logistic regression analysis was used to determine whether nuchal translucency was a significant predictor of congenital heart defect. **RESULTS:** There were 8167 chromosomally normal pregnancies, of which 21 cases of major congenital heart defect were identified at follow-up examination (incidence, 2.6/1000 pregnancies). The risk of congenital heart defect rose with increasing nuchal translucency measurements. The mean nuchal translucency value for the normal and congenital heart defect groups were 1.5 mm and 1.9 mm, respectively (P = .05). With a nuchal translucency measurement of < 2.0 mm, the incidence of congenital heart defect was 13 of 6757 pregnancies (1.9 of every 1000 pregnancies). At 2.0 to 2.4 mm, the incidence was 5 of 1032 pregnancies (4.8 of every 1000 pregnancies). At 2.5 to 3.4 mm, the incidence was 2 of 335 pregnancies (6.0 of every 1000 pregnancies). At > or = 3.5 mm, the incidence was 1 of 43 pregnancies (23 of every 1000 pregnancies). Logistic regression analysis confirmed that nuchal translucency was associated significantly with congenital heart defect (odds ratio, 2.1; 95% CI, 1.4-3.1; P = .0004). **CONCLUSION:** Increased first trimester nuchal translucency measurement was associated with a higher risk of major congenital heart defect in chromosomally normal pregnancies. The practical implications of our findings are that patients with unexplained elevations of nuchal translucency may need referral for a fetal echocardiogram.


**OBJECTIVE:** To define the prevalence of major cardiac defects according to nuchal translucency (NT) thickness at the 11 to 13 + 6-week scan in fetuses with normal karyotype. **METHODS:** Specialist fetal echocardiography was carried in 6921 fetuses with normal or presumed normal karyotype at a median gestation of 20 (range 12-35) weeks. The indications for fetal echocardiography were increased NT thickness (n = 3444), detailed second-trimester scan either for assessment of risk of chromosomal abnormalities (n = 2980) or previous or family history of fetal defects (n = 497). The cardiac defects were grouped into six functional categories: septal defect, left inflow obstruction, right inflow obstruction, left outflow obstruction, right outflow obstruction and other. **RESULTS:** Major cardiac defects were identified in 132 (19.1 per 1000) fetuses and the prevalence increased with fetal NT thickness from 4.9 per 1000 in those with NT below the median, to 8.7 for NT between the median and less than the 95th centile, 18.2 for NT between the 95th and 99th centiles, and exponentially thereafter to 35.2, 64.4 and 126.7 for respective NTs of 3.5-4.4 mm, 4.5-5.4 mm and > or = 5.5 mm. There was no obvious
difference in the distribution of NT in the different types of cardiac defects. CONCLUSIONS: The prevalence of major cardiac defects increases exponentially with fetal NT thickness and in fetuses with NT of 3.5 mm or more it is higher than in pregnancies with a family history of cardiac defects. Copyright 2005 ISUOG. Published by John Wiley & Sons, Ltd.


OBJECTIVE: The purpose of this study was to examine prospectively the association between increased nuchal translucency thickness and major cardiac defects in chromosomally normal fetuses. STUDY DESIGN: A prospective cohort study of 263 chromosomally normal fetuses with an increased nuchal translucency thickness at 11 to 14 weeks of gestation at a tertiary referral center was performed. The incidence of major cardiac defects was examined in relation to the fetal nuchal translucency thickness at the 11 to 14 week ultrasound examination. RESULTS: The nuchal translucency thickness measurements ranged from 2.2 to 8.0 mm (median, 3.1 mm). There were 13 cases of major cardiac defects in this cohort, which gave a prevalence of 49.4 of every 1000 fetuses. With the use of the 99th percentile of nuchal translucency thickness, the prevalence rose to 106.7 of every 1000 fetuses. CONCLUSION: In this population of chromosomally normal fetuses with an increased nuchal translucency thickness, the incidence of cardiac defects was high, which suggests that fetal echocardiography is indicated in this group.


Increased nuchal translucency is the strongest single marker for chromosomal abnormality. Consequently, it is currently becoming established as the foundation of most early screening programmes for Down syndrome. In the absence of chromosomal abnormality, increased nuchal translucency has been shown to be associated with other congenital anomalies including cardiac defects. Several datasets have now reported this association and here these are reviewed to assess the effectiveness of nuchal translucency measurement as a screening tool for the prenatal detection of congenital heart disease. Copyright 2004 John Wiley & Sons, Ltd.


OBJECTIVE: To determine the accuracy and practicality of fetal echocardiography in the identification of structural and functional cardiac abnormalities prior to 16 weeks' gestation in fetuses with increased nuchal translucency thickness (NT). METHODS: Between January 1996 and June 2002 early fetal echocardiography using the transvaginal route was performed at 12-16 weeks' gestation on 275 fetuses with increased NT. The abnormal cardiac findings were classified as either structural (congenital heart defects) or functional, defined as transient phenomena which might later disappear, such as isolated tricuspid regurgitation and an enlarged ascending aorta. The abnormal findings were related to pregnancy outcome, including autopsy results, karyotyping results, and late fetal and neonatal echocardiography. RESULTS: Cardiac abnormalities were present in 61 fetuses overall (22.2%); including structural cardiac defects in 37 fetuses (13.5%) and functional abnormalities in 24 fetuses (8.7%). Structural cardiac abnormalities were associated with abnormal karyotype in 24 fetuses and normal karyotype in 13 fetuses. Of the 24 fetuses with functional cardiac abnormalities, 2 (8.3%) had isolated tricuspid regurgitation and 22 (91.7%) had enlarged ascending aorta. Abnormal karyotype was present in this group in 4 cases (16.7%). CONCLUSION: Increased NT can be used to define a high-risk group that should receive specialized early fetal echocardiography. This is a reliable technique with great potential for the diagnosis of both structural and functional cardiac abnormalities. Copyright 2003 ISUOG. Published by John Wiley & Sons, Ltd.


OBJECTIVE: Increased first-trimester nuchal translucency (NT) is a possible marker for congenital heart defects in euploid fetuses. In this study, we wanted to determine the sensitivity for congenital heart defects using the 95th centile of the NT as a cut-off point. METHODS: All women who booked for delivery in our hospital in the first trimester underwent NT measurement at a crown-rump length (CRL) of between 35 and 75 mm. In all euploid fetuses and newborns with isolated or associated CHD, NT was examined retrospectively and classified as normal (<95th centile according to CRL-dependent centiles in our own data) or increased (> or =95th centile).
Detection of cardiac anomalies by nuchal translucency plus an additional test (8)


**OBJECTIVES:** To assess which was the best ductus venosus (DV) blood flow parameter to be combined with nuchal translucency (NT) in the detection of major cardiac defects at 11-13 weeks

**METHOD:** During an 8-year period (2002-2009), chromosomally normal singleton pregnancies in which fetal NT and the DV blood flow were assessed at 11-13 weeks and the fetal outcome was known were included in the study. Early fetal echocardiogram was performed when a cardiac defect was suspected or when an increased NT or an abnormal DV blood flow were observed. The detection rate and false-positive rate were calculated for major cardiac defects, considering several screening strategies: NT, DV pulsatility index for veins (PIV) above a fixed centile; DV with absent or reversed A-wave; or DV A-wave above a fixed centile, and combinations of these.

**RESULTS:** The study population included 37 cases with major cardiac defects (and normal chromosomes) and 13,064 unaffected fetuses. Fetal NT was above the 95th or the 99th percentile in 40% and 27% of major cardiac defects, respectively, and absent or reversed DV flow was observed in 39% (with 1.8% false positive rate). A 58% detection rate with a 6.7% of false positive rate was achieved when considering absent/reversed DV or NT above 95th centile. CONCLUSIONS: Adding DV blood flow parameters improves the screening efficacy for major cardiac defects in first trimester chromosomally normal fetuses.


**Objective:** To estimate the potential value of fetal assessment for tricuspid regurgitation at 11-13 weeks of gestation in the prediction of major cardiac defects. **Methods:** We screened for aneuploidies by measuring fetal nuchal translucency thickness as well as assessing blood flow across the tricuspid valve for evidence of tricuspid regurgitation and in the ductus venosus for evidence of reversed A-wave at 11 0/7 to13 6/7 weeks of gestation. The estimated performance of different combinations of increased fetal nuchal translucency, tricuspid regurgitation, and ductus venosus reversed A-wave in screening for major cardiac defects was examined. Results: The study population of euploid fetuses included 85 cases with major cardiac defects and 40,905 with no cardiac defects. Fetal nuchal translucency above the 95th percentile, tricuspid regurgitation, or ductus venosus reversed A-wave was observed in 30 (35.3%), 28 (32.9%), and 24 (28.2%) of the fetuses with cardiac defects, respectively, and in 1,956 (4.8%), 516 (1.3%), and 856 (2.1%) of those without cardiac defects. Any one of the three markers was found in 49 of the fetuses with cardiac defects (57.6%, 95% confidence interval [CI] 47.0-67.6%) and in 3,265 of those without cardiac defects (8.0%, 95% CI 7.7-8.2%). Conclusion: Assessment of flow across the tricuspid valve improves the performance of screening for major cardiac defects by fetal nuchal translucency and ductus venosus flow. 2011 by The American College of Obstetricians and Gynecologists. Published by Lippincott Williams & Wilkins.


**OBJECTIVE:** Many studies have shown that an increased nuchal translucency (NT) may be a good marker of fetal heart malformation, but the extent to which NT is suitable for identifying the population at risk remains unclear. We aimed to determine the value of NT measurement and of the presence of cystic hygroma colli in the screening of euploid fetuses for congenital heart defects (CHD). **METHODS:** We carried out a retrospective analysis of 12 910 euploid pregnancies examined between January 1995 and August 2007 at our institution. The screening performance of NT measurements in identifying fetuses with CHD was assessed, with comparison between the use of cut-offs defined as absolute values, multiples of the median (MoM) and percentiles.
presence of cystic hygroma colli was also assessed in the prediction of CHD. RESULTS: The incidence of major CHD was 3.4 per thousand (44/12,910). The sensitivity of NT measurement in screening for major CHD was 54.5% if the threshold was set at the 95(th) percentile, 45.4% if it was set at 3 mm, 27.3% for 3.5 mm, 50.0% for 1.5 MoM and 45.5% for 1.75 MoM. The false-positive rates for these thresholds were 8.4, 6.6, 1.7, 8.9 and 6.3%, respectively. The incidence of major CHD was 1.2% (10/813) in cases of thick NT (> 95(th) centile) and 4.3% (13/304) in cases of hygroma colli. CONCLUSIONS: NT measurement during the first trimester is potentially useful for screening for fetal major CHD. Screening performance is consistent whether NT values are expressed as MoMs, percentiles or absolute values. The incidence of major CHD seems to be higher in cases of cystic hygroma colli. (c) 2010 ISUOG. Published by John Wiley & Sons, Ltd.

UNLABELLED: Cardiac defects, the most common forms of congenital defects, are found in 3-8 of every 1000 pregnancies. Currently only 15-30% of CHD in newborns is detected prenatally. There are different strategies to increase the prenatal detection of cardiac abnormalities. Nuchal translucency screening and ductus venosus blood flow have been suggested to be useful methods of identifying cardiac anomalies in chromosomally normal fetuses. OBJECTIVE: To examine the association between nuchal translucency thickness and ductus venosus blood flow between 11-13.6 week of pregnancy and CHD in chromosomally normal fetuses. MATERIAL AND METHODS: Patients with singleton pregnancies at 11 to 13.6 weeks of gestation were recruited to undergo nuchal translucency sonography. The prevalence of major cardiac defects was determined and the utility of screening for nuchal translucency thickness including sensitivity, specificity, and positive and negative predictive values, were calculated for the NT thickness cut off points of the 95th and 99th centile for CRL. Ductus venosus Doppler ultrasound blood flow velocity waveforms were obtained at 10-13.6 weeks gestation. RESULTS: 4720 gestations were analyzed, of which 13 newborn infants had CHD. The incidence of major CHD increased with increasing NT. Sensitivity specificity and positive predictive values were 45.4%, 92% and 1.5% at 99.8th percentile, and 25%, 98.5%, 3.2% and 99.8% at 99th percentile. Reverse or absent flow during atrial contraction was observed in 8 out of the 13 (61.5%) chromosomally normal fetuses with CHD. CONCLUSION: Measurement of fetal nuchal translucency thickness and ductus venosus blood flow at 11-13.6 weeks of pregnancy is a sensitive method of screening for CHD. The prevalence of CHD increases with increasing fetal NT and abnormal ductus venosus blood flow. Increased NT or abnormal ductus venosus blood flow is a strong indication for fetal echocardiography.

OBJECTIVE: The purpose of this series was to determine the sensitivity of ultrasonography in early gestation (UEG) using nuchal translucency (NT) and the 4-chamber view (4CV) in the early diagnosis of congenital heart defects (CHDs). METHODS: This was a retrospective chart review of all patients presenting for UEG between 2002 and 2009. At our center, a survey of fetal anatomy is performed at the time of the NT assessment at 11 weeks to 13 weeks 6 days. A second-trimester scan (STS) is done at 20 to 23 weeks and a third-trimester scan at 32 to 35 weeks. Suspected cases of CHDs were evaluated by a pediatric cardiologist. All neonates were examined at birth by a pediatrician, and when clinically indicated, fetal echocardiography was performed. RESULTS: A total of 1370 fetuses were scanned. Congenital heart defects were identified in 8 (0.6%). Nuchal translucency was above the 95th percentile for gestational age (GA) in 6 of 8, and the 4CV was abnormal in 6 of 8. Ultrasonography in early gestation detected 75% fetuses with CHDs, and 25% were detected by an STS. CONCLUSIONS: Our study emphasizes the importance of UEG in the detection of CHDs. In this small unselected low-risk population, UEG detected 75% of CHDs. Nuchal translucency was above the 95th percentile for GA, the 4CV was abnormal, or both in all 8 cases with CHDs.

Objectives: We evaluated the outcome of unselected 1022 fetuses with NT measured at 11-13+6 scan, also estimating the role of tricuspid regurgitation in fetuses with increased NT. Methods: We studied the genetic and clinic implications for NT measurements: <95th, 95-99th centiles, 3.5-4.4 and 4.5mm, estimating the chances of chromosomal defects, fetal death, major abnormalities and delivery of a healthy baby. We further studied 34 of
the fetuses showing values of NT above 95th centile by spectral Doppler evaluation of the tricuspid valve. Results: The prevalence increases exponentially for both chromosomal defects and fetal death from 0.20%, respectively 1.64% (NT values <95th centile) to 50%, respectively 16.66% (NT thickness >4.5 mm); the prevalence of major fetal abnormalities increased from 2.16% in those with NT below 95th centile, to 7.32% for NT between the 95th and 99th centile and exponentially thereafter to 33.33% in NT thickness >4.5mm. Tricuspid regurgitation was present in 32.35% of NT>95th centile, of whom 36.36% proved to have karyotype anomalies. In contrast, 9.09% of those without tricuspid regurgitation was found to have karyotype anomalies. Structural heart defects were detected in 5 of the 11 (45.45%) with tricuspid regurgitation and in 54.54% of those without. Conclusions: Our findings of prevalence indices confirm previous studies conducted in EU and US. Therefore we consider these data useful in counseling the parents of pregnancies with increased fetal NT and in planning the appropriate follow-up. A careful search for tricuspid regurgitation is an important aspect of the evaluation of the early fetus, as this is frequently a marker for chromosomal defects even in the absence of structural heart disease.


Objective: To determine cardiac dysfunction as a potential underlying mechanism for increased nuchal translucency (NT) in fetuses with chromosomal abnormality or heart defects. Methods: Myocardial performance index (MPI) and atrioventricular valve E/A ratios for both sides of the heart were measured by Doppler echocardiography in fetuses at 11-14 weeks' gestation. The study groups consisted of 159 normal control fetuses, 199 otherwise normal fetuses but with increased NT >= 4 mm, 142 fetuses with trisomy 21, 58 with trisomy 18, 19 with trisomy 13, 37 with Turner’s syndrome and 24 with isolated heart defects. Groups were compared using Student’s t-test and confidence intervals for differences between groups were calculated. Results: Otherwise normal fetuses with increased NT showed no difference in any of the cardiac Doppler parameters from normal controls. Mean E/A ratio was slightly but significantly increased in trisomy 21 fetuses compared with normal controls (0.604 vs. 0.578 on the right, P = 0.011; 0.581 vs. 0.542 on the left, P = 0.0001). E/A ratio was not significantly different between any of the other groups and the normals but there was a small increase in absolute E-wave velocity in trisomy 18 fetuses. MPI was significantly decreased in trisomy 21 fetuses, (0.330 vs. 0.378, P = 0.002 on the left) and also in Turner's syndrome fetuses (0.301 vs. 0.352 on the right, P = 0.04; 0.320 vs. 0.378 on the left, P = 0.034) implying better performance, but not in the other groups. Conclusions: The magnitude and/or direction of the differences shown do not support a major role for cardiac functional abnormality in the development of NT. Important cardiac dysfunction could not be demonstrated in association with increased NT in normal or abnormal fetuses. Copyright 2004 ISUOG. Published by John Wiley & Sons, Ltd.


Objective: To determine whether, in a selected high-risk population, Doppler velocimetry of the ductus venosus can improve the predictive capacity of increased nuchal translucency in the detection of major congenital heart defects in chromosomally normal fetuses at 11-14 weeks of gestation. Methods: Ductus venosus Doppler ultrasound blood velocity waveforms were obtained prospectively at 11-14 weeks of gestation in 1040 consecutive singleton pregnancies. Waveforms were classified either as normal in the presence of a positive A-wave, or as abnormal if the A-wave was absent or negative. All cases were screened for chromosomal defects by a combination of maternal age and fetal nuchal translucency thickness. In 484 cases karyotyping was performed. Those fetuses found to be chromosomally normal by prenatal cytogenetic analysis, and which had abnormally increased nuchal translucency and/or abnormal ductus venosus Doppler velocimetry, underwent fetal echocardiography at 14-16 weeks of gestation. Ultrasound examination was repeated at 22-24 weeks of gestation in all women. The sensitivity, specificity and positive and negative predictive values for the detection of major cardiac defects of increased nuchal translucency thickness alone, ductus venosus Doppler alone and increased nuchal translucency thickness in association with abnormal ductus venosus Doppler were determined. Results: In 29 of 998 fetuses presumed to be chromosomally normal, reversed or absent flow during atrial contraction was associated with increased (> 95<sup>th</sup>) centile for crown-rump length) nuchal translucency. Major cardiac defects were observed in 9 of these 29 fetuses. No other major cardiac abnormalities were found in chromosomally normal fetuses in spite of the presence of either increased nuchal translucency alone or abnormal ductus venosus velocimetry. A total of 25 cardiac malformations were observed in the population. Fifteen were associated with aneuploidy and 10 fetuses had a normal karyotype. Nine of the 10 had major cardiac anomalies and one had a ventricular septal defect. The nine cases with normal karyotype and
major cardiac anomalies had both increased nuchal translucency and abnormal ductus venosus flow velocity waveforms. Conclusion: In chromosomally normal fetuses with increased nuchal translucency, assessment of ductus venosus blood flow velocimetry could improve the predictive capacity for an underlying major cardiac defect. Copyright 2003 ISUOG. Published by John Wiley & Sons, Ltd.

Detection of anomalies (including cardiac) by nuchal translucency (17)


To assess the perinatal and pediatric outcomes up to 2 years of age in singleton karyotypically normal fetuses with increased nuchal translucency (NT) above the 99(th) percentile. Singleton fetuses with NT above the 99(th) percentile and normal karyotype scanned in our center from 2002 to 2006 were included. Work-up included first- and second-trimester anomaly scan, first- and second-trimester fetal echocardiography, and in selected cases infection screening and genetic testing. Among survivors, a pediatric follow-up up to 2 years of age was undertaken. During this 4-year period, 171 singleton fetuses with NT above the 99(th) percentile and normal karyotype were included in the study. There were seven spontaneous fetal losses, 38 terminations of pregnancy and two postnatal deaths. Among the 124 (72.5%) survivors, 12 (9.7%) were born with structural abnormalities. Neurodevelopmental follow-up was completed in 108 (87.1%) of the 124 survivors and four (3.7%) showed moderate to severe impairment. Overall, a structural abnormality or genetic syndrome was diagnosed in 50 fetuses/newborns. Prenatal diagnosis was achieved for 83.8% (31/37) of the structural abnormalities and 69.2% (9/13) of the genetic syndromes. Interestingly, a single umbilical artery was found in six fetuses with no structural defects at birth, five of which had a long-term favorable outcome (4.5%), and in one 22q11 microdeletion syndrome was diagnosed at 2 years of age. Singleton fetuses with an increased NT above the 99(th) percentile and normal karyotype showed a 63% intact survival. Long-term neurodevelopmental outcome among survivors did not appear to differ from that reported for the general population. Copyright 2011 ISUOG. Published by John Wiley & Sons, Ltd.


To determine the sensitivity of first-trimester ultrasound for diagnosing different structural anomalies in chromosomally normal pregnancies, and to establish the role of aneuploidy markers in the detection of abnormalities. This was a retrospective study of chromosomally normal singleton pregnancies with an 11-14-week scan performed in our center during 2002-2009. The ultrasound examination included an early fetal anatomy survey and assessment of nuchal translucency, ductus venosus blood flow and nasal bone. Among 13723 scanned first-trimester pregnancies with no genetic anomalies and complete follow-up, 439 fetuses (3.2%) were found to present with structural anomalies (194 with major anomalies and 245 with only minor anomalies). Forty-nine per cent of major structural anomalies were detected during the first-trimester scan, the highest rates corresponding to acrania (17/17), holoprosencephaly (three of three), hypoplastic left heart syndrome (10/10), omphalocele (six of six), megacystis (seven of eight) and hydrops (eight of nine). Higher than expected detection rates were obtained for skeletal (69%) and cardiac (57%) defects, coincidentally showing the highest presence of an increased nuchal translucency or abnormal ductus venosus blood flow (38% and 52%, respectively). The finding of an absent nasal bone did not appear to be associated with structural defects. About half of major structural abnormalities can be diagnosed in the first trimester. Increased nuchal translucency or abnormal ductus venosus blood flow appear to be associated with cardiac and skeletal defects and may facilitate early detection. Copyright 2012 ISUOG. Published by John Wiley & Sons, Ltd.


OBJECTIVE: To evaluate the ability to diagnose structural fetal anomalies during or soon after an extended nuchal translucency (NT) examination. STUDY DESIGN: The study included all women who had a routine NT examination and women who were referred following an abnormal NT examination. The sonographers were instructed to pay attention to fetal anomalies while performing the NT examination. Each examination was
initially attempted transabdominally. Failure to obtain adequate views transabdominally was an indication for a transvaginal examination. When a structural fetal anomaly was detected or suspected, a full fetal anomaly scan was performed. When diagnosis could not be established, fetal anatomy scan was repeated after 14 weeks’ gestation. Fetal cardiac scanning was performed transvaginally, immediately or within 3 days after an increased NT was observed. When fetal anomalies were diagnosed the patients were informed about the possibilities of terminating the pregnancy or continuing the work-up and follow-up. RESULTS: We performed 4467 NT examinations during the study period and additional 123 fetal cardiac scanning following an abnormal NT examination. Overall, we performed 365 fetal cardiac scanning between 11-14 weeks' gestation. The fetal anomalies detected included the following: three skeletal anomalies, seven brain anomalies, four urinary system anomalies, four abdominal anomalies, two facial anomalies, and 13 cardiac anomalies. Six of the 13 cardiac anomalies were atrioventricular canal. One third of the patients (11/33) elected to discontinue pregnancy short time after the detection of the congenital anomaly (until 14 weeks’ gestation) and half of the patients (16/33) asked for termination of pregnancy later. More than 60% of the patients (20/33) with congenital anomalies detected following the NT examination elected not to have chorionic villous sampling (CVS) or amniocentesis. CONCLUSIONS: The opportunity to scan the fetal anatomy at the early stages of pregnancy, when the NT examination is performed, justifies the approach of extended NT examination. (Figure presented).


OBJECTIVE: Large nuchal translucency (NT) is associated with a higher risk for chromosomal and structural anomalies. Our objective was to examine the role of transvaginal early anatomy ultrasound (TEAU) in the management of pregnancies with large NT. STUDY DESIGN: Data from cases who had a TEAU due to a large NT (=3.0 mm) between April 2007 and August 2009 was prospectively collected. TEAU was performed at 13-15 weeks of gestation by a single experienced physician and included detailed fetal anatomy examination. Information from the routine anatomy ultrasound, chromosomal testing, autopsy findings, and pregnancy outcome was collected prospectively. RESULTS: 68 fetuses with a large NT were examined during the study period. In 18 cases (26%), anomalies were detected during the TEAU. 13 of the 18 women were found to have fetuses with major cranial and/or cardiac anomalies and the pregnancies were terminated before the standard 19 weeks ultrasound was completed. In 5/13 who terminated, there were no chromosomal aberrations; in 8/13, chromosomal aberrations were found but only half detected by FISH. Of the 5 women with fetal anomalies who continued with the pregnancy, there were 2 cases of IUFD, 1 case of Down Syndrome, and 2 cases with mild, non-lethal abnormalities. In total, 9 cases of chromosomal aberrations were diagnosed and all were found to have fetal structural anomalies. Three cases had an abnormal outcome not detected by TEAU or by the routine anatomy scan. TEAU had a 95% detection rate of ultrasound-detectable fetal anomalies when compared to pregnancy outcome. TEAU was significantly more effective in detecting abnormal outcome compared to chromosomal testing (86% vs 43%, p<0.05). CONCLUSIONS: First trimester targeted TEAU of fetuses with an increased NT is highly effective in detecting fetal anomalies and can contribute to timely parental decision regarding the future of the pregnancy, especially when a structural anomaly is diagnosed. Fetal anomalies are common in fetuses with large NT and therefore TEAU is suggested as the first line investigation in the management of the condition.


Objective: To examine the performance of the 11-13 weeks scan in detecting non-chromosomal abnormalities. Methods: Prospective first-trimester screening study for aneuploidies, including basic examination of the fetal anatomy, in 45 191 pregnancies. Findings were compared to those at 20-23 weeks and postnatal examination. Results: Aneuploidies (n = 332) were excluded from the analysis. Fetal abnormalities were observed in 488 (1.1%) of the remaining 44 859 cases; 213 (43.6%) of these were detected at 11-13 weeks. The early scan detected all cases of acrania, alobar holoprosencephaly, exomphalos, gastrochisis, megacystis and body stalk anomaly, 77% of absent hand or foot, 50% of diaphragmatic hernia, 50% of lethal skeletal dysplasias, 60% of polydactyly, 34% of major cardiac defects, 5% of facial clefts and 14% of open spina bifida, but none of agenesis of the corpus callosum, cerebellar or vermian hypoplasia, echogenic lung lesions, bowel obstruction, most renal
defects or talipes. Nuchal translucency (NT) was above the 95th percentile in 34% of fetuses with major cardiac defects. Conclusion: At 11-13 weeks some abnormalities are always detectable, some can never be and others are potentially detectable depending on their association with increased NT, the phenotypic expression of the abnormality with gestation and the objectives set for such a scan. Copyright 2011 John Wiley & Sons, Ltd.


OBJECTIVE: To determine the relationship between nuchal translucency (NT) thickness and the risk of structural fetal abnormalities

STUDY DESIGN: We performed a retrospective cohort study of all cases of non-septate NT measurements greater than or equal to 2.5 mm during first trimester screening from 2000-2010 at five referral centers. Comparison was made to a random group of patients with a NT < 2.5mm found during the 10 year time period. Medical records of these cases were reviewed for ultrasound findings of structural abnormalities.

RESULTS: The incidence of structural abnormalities increased based on NT size (Table 1). Among fetuses with structural abnormalities, 30% had major cardiac anomalies, 22% had genitourinary abnormalities, and 25% had central nervous system abnormalities. CONCLUSIONS: Increasing NT measurements, specifically with a NT <3mm, are associated with increased risk of structural abnormalities. These findings may be helpful in counseling patients with abnormal NT findings on first trimester screening. (Table presented).


OBJECTIVES: To evaluate the perinatal and pediatric outcome up to two years of age in singleton fetuses with increased nuchal translucency (NT) and normal karyotype.

METHODS: We reviewed the singleton pregnancies undergoing a first trimester scan from 2002 to 2006. In fetuses with NT above the 99th percentile and normal karyotype, work-up included first and second trimester anomaly scans, fetal echocardiography and in selected cases infection screening and genetic tests. Pediatric follow-up up to 2 years of age. An adverse outcome included miscarriage, intrauterine death, termination of pregnancy and the finding of structural defects or genetic disorders.

RESULTS: During this period, 171 singleton fetuses with NT > 99th percentile and normal karyotype were studied. There were 7 fetal demises, 2 postnatal deaths and 38 terminations of pregnancy. Among the 124 (73%) survivors, 112 (66%) were born with no defects. Overall, 48 fetuses had structural abnormalities: 22 cardiac defects, 5 hydrops, 3 urinary defects, 2 skeletal defects, 2 central nervous system defects, and 1 pterygium multiple. There were 12 fetuses with genetic syndromes and one with a fetal akinesia deformation sequence. Prenatal diagnosis was achieved in 30 (83%) structural abnormalities and 10 (83%) genetic syndromes. Interestingly, there were 6 (5.5%) fetuses with a single umbilical artery, but only one was associated to a malformative disorder. Neurodevelopmental follow-up was completed in 96 (86%) of the 112 survivors with no defects. Among these, 6 (6%) showed abnormal neurodevelopment: 3 had severe impairment, one had mild language impairment, one was hypotonic and one was lost at follow-up.

CONCLUSION: Singleton fetuses with increased NT>99th percentile and normal karyotype showed a 73% postnatal survival. Among these infants, 10% had structural anomalies and 6% showed abnormal neurodevelopment.


BACKGROUND: Nuchal translucency is widely used to screen for trisomy 21 in the first trimester of pregnancy. It has also been associated with other chromosomal abnormalities, genetic syndromes and congenital defects.

OBJECTIVE: To evaluate the perinatal outcome of patients who showed nuchal translucency greater or equal to 95th percentile during the first trimester ultrasound screening, which underwent fetal karyotype.

MATERIAL AND METHOD: Case series. Fetuses with nuchal translucency greater or equal to 95th percentile were evaluated by fetal karyotype, second-trimester structural ultrasound scan, fetal echocardiography and postnatal clinical genetic evaluation, attended in the servicio de Genetica of the Instituto Nacional de Perinatologia Isidro Espinosa de los Reyes. RESULTS: 48 fetuses were evaluated. The karyotype was normal in 39 (81%) and abnormal in 9 (19%) cases of which three had trisomy 21, three monosomy X, two trisomy 18 and
In the cases with normal karyotype, 13 (33%) showed an abnormal second trimester ultrasound scan; among them, 12 had major congenital defects, 5 of them had abnormal cardiac findings that were confirmed by fetal echocardiography. In the group of 26 fetuses with normal karyotype and ultrasound, only 2 patients had minor birth defects. CONCLUSIONS: Increased fetal nuchal translucency is frequently associated with chromosomal abnormalities and several congenital defects, mostly heart defects and genetic syndromes. Our findings are in accordance with other published reports where a complete follow-up of all patients with increased nuchal translucency is recommended even if they have a normal karyotype, due to the increased risk of having other congenital defects or syndromic entities.

Scott F, Evans J, McLennan A. Perinatal outcome in fetuses with extremely large nuchal translucency measurement. The Australian & New Zealand journal of obstetrics & gynaecology 2009;49 (3):254-57. BACKGROUND: Studies have suggested that an entirely normal outcome is likely when the nuchal translucency (NT) measurement is very large and the karyotype, morphology and echocardiography scans are normal. Recently this has been questioned as it is based on very small numbers. AIM: Assess the outcome of pregnancies with an NT measurement of 6.5 mm or greater. METHODS: Audit of a large first trimester screening program. RESULTS: Over the ten years to 2006, 76 813 patients underwent first trimester screening, with 120 having an extremely large NT. Thirty-one cases had normal karyotypes, of which there were four sets of twins that demised. Six cases miscarried and ten were terminated, some with morphological abnormalities. Eight cases were still alive for the morphology scan, with the only abnormality being mild pyelectasis in one case. At birth, three cases were normal and another three cases had a good outcome. Two cases had coarctation of the aorta and a good outcome. One case had Noonan's syndrome, another had cerebral palsy and the case with pyelectasis had hydronephrosis, dilated ureters and some contractures. CONCLUSIONS: When the karyotype and morphology scan are normal, the outcome is often good in spite of an extremely large NT. However, even a subtle ultrasound anomaly can indicate a genetic syndrome and echocardiography cannot exclude mild cardiac abnormalities.

Saldanha FAT, Brizot MdL, Moraes EAd, et al. Increased fetal nuchal translucency thickness and normal karyotype: prenatal and postnatal follow-up. [Portuguese]. Revista Da Associacao Medica Brasileira 2009;55(5):575-80. OBJECTIVE: The aim of this study was to evaluate pregnancy and postnatal outcomes of fetuses with increased nuchal translucency thickness (NT) and normal karyotype. METHODS: Two hundred seventy five fetuses with increased NT were examined with karyotyping analysis, serial ultrasound scans, echocardiography and postnatal clinical and genetic evaluation at the Fetal Medicine Unit - Department of Obstetrics - Sao Paulo University. RESULTS: The karyotype was abnormal in 14.2% of the cases and normal in 85.8%. In cases with normal karyotype 24.7% presented structural abnormalities at the anomaly scan, one third of these were major malformations with 35.7% of heart defects. Adverse pregnancy outcome such as miscarriages, intrauterine and neonatal deaths occurred in 10.2% of cases. Of the infants 72.7% had postnatal examination, with 14.8% presenting abnormalities. Chances of having a live and healthy child decreased with increased NT thickness, and were of 37.5% for NT above 4.5mm. CONCLUSION: In cases with increased NT thickness and normal karyotype, the frequency of fetal malformations, especially heart defects, adverse pregnancy outcome and postnatal abnormalities is related to the NT thickness.

Axt-Fliedner R, Hartge D, Chiriac A, et al. Long-term outcome for children born after a first-trimester measurement of increased nuchal translucency with a normal karyotype: a retrospective analysis. Ultrason in der Medizin 2009;30(6):558-63. PURPOSE: To study the outcome of pregnancy in chromosomally normal fetuses with increased nuchal translucency with respect to fetal loss, structural defects genetic syndromes, and neurological outcome. MATERIALS AND METHODS: Retrospective analysis and telephone interview. All included pregnancies underwent a mid-trimester anomaly scan. RESULTS: 279 pregnancies were included. The overall live birth rate was 81.4 %, and decreased as the NT measurement increased. The most common structural defect was cardiac anomalies (7 %). If the second-trimester anomaly scan was uneventful, the chance of a healthy live birth was 92 %. The number of unexpected neurodevelopmental delays after a normal scan during mid-trimester was 1.1 %. CONCLUSION: Counseling should emphasize that if the karyotype is normal and no fetal structural malformations were missed prenatally after resolution of nuchal thickening, the prognosis is positive. Georg Thieme Verlag KG Stuttgart, New York.

OBJECTIVES: The aims of this study were to review detection of fetal malformations during the first trimester and to study pregnancy and infant outcomes. We wanted to check if the lengthening of the legal delay for voluntary termination of pregnancy changes the outcome of the pregnancy, in cases outside of the legal requirements. MATERIALS AND METHODS: This study was overseen by the French college of fetal echography (CFEF). All the cases of abnormality detected before 14 weeks' gestational age, excluding the isolated increased nuchal translucency, were extracted from the total population examined, and details were entered into the database of the French College of Fetal Echography. All case records were then analyzed. We compared two populations: before and after July 2001. RESULTS: We observed 336 fetuses with malformation(s), 108 before July 2001 and 208 after that date. One percent (0.5-1.6) of scans performed between 10 and 14 weeks revealed fetal abnormalities apart from isolated increased nuchal translucency. Of the 336 cases retained for investigation, 109 increased nuchal translucency or hygroma associated with other malformation(s), 103 central nervous system anomalies, 85 malformations of the thoracoabdominal wall, 81 limb abnormalities, 41 had renal malformations, 28 spinal abnormalities, 21 had heart malformations, 16 involved biometric abnormalities, 12 involved abnormalities of the appendages, and 11 facial abnormalities. Medical termination of pregnancy was performed in 75% of cases. Death in utero occurred in 9% of cases, 12% of infants were born alive. In 3.9% of cases, an abortion was performed. There were no differences between both populations before and after July 2001. CONCLUSION: Excluding isolated increased nuchal translucency or hygroma, malformation before 14 weeks' gestational age was detected in 1% of fetuses. The most common malformations detected in the first trimester were non-isolated increased nuchal translucency and malformations of the thoracoabdominal wall and the brain. The prognosis for fetuses with malformations detected during the first trimester was very poor as only 12% of these infants were born alive, some of them with severe malformations. In our study, and given its limitations, there were no differences between the number of voluntary terminations performed before and after July 2001.


Objective: The purpose of this study was to evaluate the ability to screen for structural fetal anomalies during the nuchal translucency (NT) ultrasound examination, without performing a complete anatomic fetal scan, by using the sagittal views of the fetus. Study Design: In a prospective study, we evaluated all the suspected structural findings observed during the NT examinations performed in our Division of Maternal-Fetal Medicine in 2004-2005. The purpose of the examination was to screen for fetal chromosome abnormalities by using the fetal NT measurements. However, the sonographers were instructed to pay attention to any abnormality observed while obtaining the sagittal views of the fetus. Other views were not to be obtained and fetal anatomy scan was performed only if a structural fetal anomaly was suspected when viewing the fetus in sagittal planes. When a structural fetal anomaly was suspected, a fetal anatomy scan was performed, and then a diagnosis was established at 14-16 weeks' gestation or later. Results: We performed 1723 NT examinations during the study period. The sonographers suspected structural fetal anomalies in 22 cases (1.3%), most of them performed between 11.2 and 13 weeks' gestation. Further evaluation of these cases diagnosed 9 fetuses (0.52%) with structural anomalies including: acrania, holoprosencephaly, Dandy-Walker syndrome, cerebellar agenesis, prune belly syndrome, 2 cases of omphalocele, and 2 cases of cleft lip. The NT was abnormal (greater than 3 mm) in only 1 case (omphalocele). None of the additional 8 cases diagnosed with structural anomalies had a positive maternal serum screening result for trisomy 21. Eight of these 9 fetal structural anomalies were sonographically confirmed at 14-16 weeks' gestation and the remaining 1 was confirmed at 20 weeks' gestation. An additional 13 noncardiac structural anomalies were detected in the study group during routine fetal anatomy scan performed at 14-16 or at 18-24 weeks' gestation. Four of these 9 fetal cardiac defects (44%) were diagnosed by an early fetal echocardiography performed for an increased fetal NT. Conclusion: In addition to chromosomal anomalies and congenital cardiac defects, the NT examination can provide an opportunity to screen for structural fetal anomalies when viewing within the sagittal planes of the fetus. The NT examination can be used as a screening test for those who require an early fetal anatomy scan without performing an additional early anatomy scan to all patients. 2007 Mosby, Inc. All rights reserved.

Objectives: To study the outcome of pregnancy in chromosomally normal fetuses with increased nuchal translucency thickness (NT), with respect to fetal loss, structural defects and genetic syndromes with developmental delay, and to provide information that would be helpful for parental counseling on the residual risk of adverse outcome when ultrasound findings are normal. Methods: We reviewed the outcome of all pregnancies presenting at the Academic Medical Centre in Amsterdam with increased NT between January 1994 and March 2005. Fetal karyotyping and two-step ultrasound investigation at 13-18 and 20-24 weeks' gestation were offered in all cases. Particular attention was paid to the relationship between normal karyotype, ultrasound findings at the 20-24-week scan and subsequent pregnancy outcome. An adverse outcome was defined as miscarriage, intrauterine death, termination of pregnancy at parental request or the finding of one or more structural defects or genetic disorders. Results: A total of 675 fetuses with increased NT, known karyotype and known pregnancy outcome was analyzed. A chromosomal anomaly was detected in 224 (33%) fetuses. In 451 (67%) fetuses, the karyotype was normal. The overall incidence of an adverse pregnancy outcome in this group was 19% and, when analyzed according to the initial degree of increase in NT, the likelihood of an adverse outcome increased with increasing NT, ranging from 8% to 80%. 425 fetuses underwent a detailed second-trimester ultrasound scan. Anomalies were detected, at the time of ultrasound or after birth, in 54 (13%) of these fetuses (17 isolated cardiac defects, 14 other structural defects and 23 genetic disorders). An adverse pregnancy outcome was recorded in 4% of cases in which there were normal findings at the 20-week scan. Seven of these cases were classified as 'potentially amenable' to ultrasound detection. With exclusion of these cases, the chance of a healthy baby, if the 20-week scan was completely normal, was 98%. Genetic syndromes with dysmorphic features and neurodevelopmental delay occurred in seven (1.6%) of the fetuses with normal karyotype. In three of these pregnancies, non-specific suspicious ultrasound findings (nuchal edema, mild pyelectasis, pericardial effusion) were observed at the mid-trimester scan and in two others, subtle cardiac defects were detected after delivery. In the remaining two cases (0.5%) the mid-trimester scan was completely normal and no structural defects were observed after delivery. Conclusion: After exclusion of chromosomal anomalies, one out of five fetuses with increased NT has an adverse pregnancy outcome. The chance of an uneventful pregnancy outcome depends on the initial degree of increase in NT. However, if the detailed ultrasound examination at around 20 weeks is normal, a favorable outcome can be expected with confidence, irrespective of initially increased NT. Copyright 2007 ISUOG. Published by John Wiley & Sons, Ltd.


AIMS: The number of fetuses with an abnormal increased first trimester nuchal translucency (NT), but confirmed normal karyotype and anatomy is relatively small and therefore a challenge for prenatal counseling. Universal guidelines are still needed for a systematic work-up, how to decide on the rewarding cut-off for this policy as well as how to counsel patients with an increased NT but with euploid fetuses. The current review aims to address some of these issues. RESULTS: Eleven studies reporting on the pregnancy outcome of 2,128 euploid fetuses with increased NT (>or=3 mm or >or=95 centile) were retrieved by our previously reported literature search. 2.2-10.6% of the fetuses has miscarried and 0.5-15.8% ended in perinatal death. There was an overall rate of 0.5-13% neurodevelopmental problems, and 2-8% of the malformations were undiagnosed before birth, the most common being cardiac anomalies. Nevertheless, 70-90% fetuses had normal outcomes. CONCLUSION: For those euploid fetuses with increased NT>2 MoM or >or=1.5 mm delta NT we recommend a detailed two-step anomaly scan including midgestation fetal echocardiography. Maternal age as well as data on relevant family history and persistence of nuchal edema provides additional relevant information for counseling and planning pregnancy management. [References: 57]


The aim of this study was to investigate outcome at the age of two years for infants without known chromosomal anomalies who presented increased nuchal translucency (NT) at first trimester ultrasound examinations. One hundred fifty-one infants with NT measuring 3mm or more, between 12 and 16 weeks gestation, were followed for at least 24 months. A homogeneous pediatric examination was applied. Among these 151 infants, thirteen (8%) had a major isolated malformation. Five infants (3.3%) had chromosomal anomalies which were unrecognized on fetal karyotype owing to tissue mosaic in two and to cryptic
chromosomal anomalies in three. At the age of two years, 16 children (10%) presented psychomotor retardation as part of a genetic syndrome, half of them had an associated cardiac malformation. We did not find any specific ultrasound characteristics which could be used to distinguish fetuses with impaired neurological prognosis. Newborns who presented NT at the first trimester ultrasound examination constitute a high risk population, particularly for psychomotor retardation which is not always recognized during the neonatal period. Careful pediatric follow up is required during childhood.


BACKGROUND: In recent years, an increasing amount of experience has been collected in measuring the nuchal translucency (NT) of the fetus in early pregnancy. While all fetuses develop a measurable collection of fluid in the area of the neck between the 11th and 14th weeks of pregnancy, the fact that fetuses with chromosomal disorders, cardiac defects, and syndromal diseases, in particular, reveal an above-average incidence of increased NT has been noticed. OBJECTIVE: By processing our own patient data from the past two years, we intend to elucidate the question of whether NT measurement is a sensible investigation for the early detection of fetal problems. PATIENTS AND METHOD: NT measurements were carried out in 199 fetuses; these measurements were standardized according to the guidelines of the Foetal Medicine Foundation in London, in whose multicentric study we are participating. The patients were under the care of our prenatal diagnosis and therapy department and were referred to us from external sources. RESULTS: NT within the reference range was determined in 152 fetuses; NT exceeded the reference value in 47 fetuses. Of those fetuses with increased NT, 7 fetuses revealed a chromosomal anomaly, 1 foetus was suffering from a cardiac defect, 3 fetuses were suffering from other organ abnormalities, and 3 fetuses were determined to be suffering from syndromal disease. None of the fetuses whose NT measurements were within the reference range was discovered to be suffering from any of the above-mentioned problems. CONCLUSION: Even this relatively small group of patients reveals that NT measurement is a very effective filter for detecting certain fetal diseases during the early fetal period.

Nuchal translucency in referral for echocardiography (8)


Objectives: To evaluate trends over time, indications, diagnoses, noncardiac defects and outcome of fetuses referred for tertiary level echocardiography. Methods: Retrospective study of fetal echocardiograms performed between April 1999 and 2009. Results: Of the 623 fetuses included, 301 (48%) had cardiac pathology. Congenital heart defects (CHDs) were found in 243/301 (81%), mostly in the severe spectrum. Of the fetuses with CHDs, 26% (63/243) had chromosomal anomalies. The chromosomally normal fetuses with CHDs had a mortality rate of 43% (77/180) and 23% (41/180) had extra-cardiac anomalies. The termination of pregnancy (TOP) rate for all cardiac pathology was 24.9% (75/301) and for CHDs 29.6% (72/243). The TOP rates for CHDs diagnosed before 19 and 24 weeks gestation were 61% (28/46) and 44% (68/155), respectively. An increase in referrals followed the introduction of a national screening program, (nuchal translucency (NT) and routine structural ultrasound screening). The main referral indication was an increased NT (>95th percentile; 32% of cases). CHDs were found in 81/239 (34%) fetuses with an increased NT. Conclusions: Referral indications for fetal echocardiography were appropriate (almost 50% had cardiac pathology). The mortality was high. Fetal outcome and TOP decisions correlated with CHD severity and presence of noncardiac defects. An increased NT is a strong marker for CHDs. 2011 John Wiley & Sons, Ltd.


OBJECTIVE: The aim of the study was to evaluate the indications and outcomes of fetal echo (FE) and determine which indication has the highest detection rate for congenital heart disease (CHD). METHODS: The referral indications and results of FE performed in Iceland during 2003-2007 were reviewed. Information regarding gestational age at diagnosis, nuchal translucency, pregnancy outcome, autopsy results and postnatal diagnosis were obtained from medical records. RESULTS: During the five year period 1187 FE were performed. Structural heart defect was diagnosed in 73 fetuses. The most common referral indication was family history of CHD (631;53.2%) which led to diagnosis of 18 heart defects prenatally (2.9%). The second most common referral indication was increased nuchal translucency (159) and abnormal cardiac findings were present in 16 cases (10.1%). A total of 30 women were referred for FE because of abnormal four chamber view (AFCV) which resulted
in the diagnosis of 22 (73.3%) major heart defects, either incompatible with life or requiring immediate intervention after birth. Other indications led mostly to the diagnoses of minor defects. CONCLUSIONS: AFCV is the most important predictor for diagnosis of structural heart defects. 2.5% were referred for FE due to AFCV which led to diagnosis of 30% of all heart defects, all of which were major. Key words: fetal echocardiography, indications, congenital heart disease.


To examine prospectively the reliability of ultrasound-trained obstetricians performing a first-trimester fetal cardiac scan with high-frequency transabdominal probes, by confirming normal or abnormal heart anatomy, in pregnancies referred for increased nuchal translucency thickness (NT). Trained obstetric operators assessed the fetal heart in 133 fetuses with increased NT (> 95th centile) at 11-14 weeks of gestation. A high-frequency transabdominal probe was used to confirm or refute normal cardiac anatomy rather than to establish a specific diagnosis. Following this preliminary screening by the ultrasound-trained obstetrician, specialized fetal echocardiographers rescanned the fetal heart in order to confirm the accuracy of the obstetric operators' findings and to establish a diagnosis in abnormal cases. Fetal cardiologists repeated the examinations at 20 and 32 weeks of pregnancy. Postnatal follow-up lasted 2 years. Twelve fetuses with normal karyotype and normal anatomy were lost to follow-up. A total of 121 fetuses with increased NT between 11 and 14 weeks’ gestation were studied. Congenital heart disease (CHD) was detected in 20/121 (16.5%) fetuses. In addition, there were three with mild ventricular disproportion, the right ventricle being larger than the left, considered as a minor non-specific cardiac abnormality. CHD was associated with chromosomal anomalies in 12/20 (60%) cases. Among the 121 fetuses, there was agreement between ultrasound-trained obstetricians and fetal cardiologists in 116 (95.9%) of the cases, and the ultrasound-trained obstetricians correctly identified 18 cases with major cardiac defects. However, there was disagreement in five cases: two with small ventricular septal defects and three with ventricular disproportion. Our results provide evidence that obstetricians, trained to study the heart in the second trimester, can also differentiate reliably between normal and abnormal heart findings in the first trimester, when using a high-frequency transabdominal ultrasound probe. (c) 2010 ISUOG. Published by John Wiley & Sons, Ltd.


Objectives To analyze the main prenatal characteristics of hypoplastic left heart syndrome (HLHS), its association with extracardiac anomalies including increased nuchal translucency (NT) and the outcome of affected patients. Methods We searched our database for classical forms of HLHS (aortic atresia, mitral and aortic atresia and critical aortic stenosis evolved to a severely hypoplastic left ventricle) prenatally diagnosed between 1998 and 2006. Data on 101 fetuses were retrieved and analyzed. Results The main reason for referral was suspected heart defect on a routine ultrasound scan (82%). The mean gestational age at diagnosis was 21 weeks. Most cases were detected at <=22 weeks (72%), the upper limit for termination of pregnancy (TOP) in our country (Spain). An intact atrial septum was diagnosed in 11 of the 58 fetuses (19%) in which pulmonary vein blood flow was assessed, and this diagnosis was proved to be correct in the six liveborn babies. Most fetuses (68%) had an isolated HLHS. Fourteen fetuses (14%) were chromosomally abnormal and all had associated extracardiac defects. NT was above the 95th centile in 21 of the 74 cases (28%) in which this measurement was available. 79% (58/73) of the cases in which HLHS was detected at =22 weeks were terminated, and no differences in the rate of TOP were found through the study period. Among the 43 continuing pregnancies, seven fetuses died in utero and there were 36 live births; in 12 cases the parents opted for compassionate care and 24 chose to have the infant surgically treated. In the cohort of intention-totreat cases, the overall survival rate was 36% (9/25). This rate improved from 18% (2/11) in the period 1998-2002 to 50% (7/14) in 2003-2006. There were no survivors in cases with intact atrial septum or when there were associated defects. At follow-up, 2/9 survivors suffered from significant neurological morbidity. Conclusions Fetal echocardiography allows an accurate diagnosis of HLHS, which is made in most instances in the first half of pregnancy. Despite the advantage offered by the prenatal detection of HLHS, which provides the opportunity to plan perinatal management, our up-to-date results show that the outlook for these fetuses is still poor, and highlight the importance of presenting these figures when counseling parents with affected fetuses. 2009 ISUOG.

Objective: To study the implications of early fetal cardiac scanning immediately following an abnormal nuchal translucency (NT) examination. Methods: Fetal cardiac scanning was performed immediately after an increased NT was observed. Scans were performed transvaginally at 11 to 14 weeks. Fetal echocardiography was repeated between 14 and 24 weeks in continuing pregnancies, or when the cardiac scanning appeared normal at 11 to 14 weeks. Results: We performed 2513 NT examinations. An abnormal NT was observed in 135 (5.4%) patients. In addition, 65 patients with an abnormal NT were referred to us for fetal cardiac scanning from other offices. Overall, we performed 200 fetal cardiac scans between 11.2 and 13.5 weeks for an abnormal NT examination. Twelve major fetal cardiac anomalies were diagnosed between 12 and 13.5 weeks. Seven patients (58%) terminated pregnancy between 12 and 14 weeks without performing chorionic villous sampling (CVS). Five patients asked for chromosomal analysis before deciding about their pregnancy. Fetal cardiac anomalies were suspected in six additional cases, but only one of them was diagnosed. Another five minor and one major fetal cardiac anomaly were suspected at 11 to 14 weeks but diagnosed later on fetal echocardiography. Conclusion: Major fetal cardiac anomalies can be detected immediately following an abnormal NT examination and be useful for the patients' decisions about the management of their pregnancy. Copyright 2008 John Wiley & Sons, Ltd.


The development of high-resolution ultrasound machines with high-frequency transvaginal and transabdominal probes as well as use of color Doppler echocardiography have made it possible to evaluate fetal heart status in detail as early as the end of the first trimester and beginning of the second trimester of pregnancy. Early fetal echocardiography not only requires extensive knowledge of early fetal cardiac anatomy and awareness of technical limitations, but also expertise in the field of transvaginal sonography. These prerequisites are usually only met in specialized centers so that its use is limited to groups at risk of congenital heart abnormalities. The prevalence of congenital heart defects is 5-8 per 1000 live births, making them the most frequent of severe congenital malformations. Because of the high lethality in fetuses with severe deformities, especially chromosomal aberrations and cardiac defects, prevalence during the first trimester is likely to be 15-20 per 1000 fetuses. The classic indications for fetocal echocardiography are supplemented by evidence of increased nuchal translucency in early pregnancy since measurement of nuchal translucency between the 11th and 14th week of gestation serves to identify fetuses not only at increased risk of chromosomal anomalies but also of congenital heart defects. The prevalence of defects increases in tandem with nuchal thickness. Increased nuchal translucency thickness is associated with a higher risk of heart defects than many other established indications for echocardiography. Admittedly, however, only 10-20% of severe cardiac defects exhibit increased nuchal translucency during early pregnancy so that the detection rates for cardiac defects are much lower than with a detailed four-chamber view on imaging during the second trimester (40%) and the combination of four-chamber view and imaging of the outflow tract in the second trimester (70%). Doppler examination of the ductus venosus between the 11th and 14th week of gestation can provide additional information since an association between abnormal blood flow patterns in the ductus venosus and cardiac defects in fetuses with increased nuchal translucency and normal karyotype has been described. Since structural anomalies of the fetal heart and the large vessels only become manifest in the later course of pregnancy, even when imaging evidences normal cardiac anatomy and normal blood flow pattern, a further echocardiographic examination is necessary around the 20th week of gestation, as is the case in all indications for echocardiography.


Objectives: We hypothesized that increased facility with fetal echocardiographic diagnosis by obstetricians is associated with changes in its indications and yields. Methods: We reviewed 300 fetal echocardiograms (December 2002-August 2003) and compared our findings with previous studies. Results: Mean maternal age was 31 +/- 6 (range 16-44) years. Gestational age was 24 +/- 5 weeks (mean +/- SD; median 22, range 15-38). Indications for fetal echocardiography included family history of congenital heart disease (CHD) (23%), maternal diabetes (18%), obstetrical scan suspicious for CHD (13%), arrhythmia (12%) maternal rheumatologic disease (7%), extracardiac congenital anomalies (6%), chromosomal anomaly (6%) and exposure to a potential fetal teratogen (5%). High yield indications included chromosomal anomaly (47%) and a suspicious obstetrical scan (42%). Low yield indications included family history of CHD (4%) and teratogen exposure (0%), 1/7 of the patients
with increased nuchal translucency had pulmonary atresia/intact ventricular septum. No anomalies were associated with the single umbilical artery. Conclusion: Indications and yields of fetal echocardiography have changed over the last decade. The frequency of an obstetrical scan suspicious for CHD has increased 2.5 to 3 times over a decade and continues to have high yield. Thus, increasing prenatal detection of CHD depends, to a large extent, on increasing the skills of obstetricians. Copyright 2004 John Wiley & Sons, Ltd.


Objective: To examine the prevalence, distribution and spectrum of cardiac defects in chromosomally normal fetuses with increased nuchal translucency thickness. Patients and methods: During a 4-year period, targeted fetal echocardiography was used in 353 chromosomally normal fetuses with increased nuchal translucency thickness at 10-14 weeks' gestation. The cardiac scan was performed at 18-22 weeks. In the last 138 cases enrolled, an additional scan at 12-16 weeks was carried out. The follow-up included the findings at necropsy or in the pediatric examination. A complete follow-up was achieved in 97%. Results: Cardiac defects were present in 32 (9.1%) cases, increasing from 5.3% in those with a nuchal translucency thickness of >=95th centile (3.9 mm) to 24% when thickness >=6 mm (p< 0.001). In 31 cases (97%), the cardiac defect was diagnosed antenatally; in 24 cases (77%) this diagnosis was confirmed later. In the remaining seven cases, the autopsy examination was not available. A wide range of cardiac defects was observed, with the most common being atrioventricular septal defect and tricuspid atresia. Conclusions: Euploid fetuses with increased nuchal translucency thickness have a significantly increased risk of cardiac defects. This is a marker of different types of heart anomalies and constitutes an additional indication for targeted fetal echocardiography. Most of the cardiac defects can be detected by fetal echocardiography.